

**AMENDMENTS TO THE CLAIMS**

1. (Currently Amended) A method for ~~in vivo down-regulation of autologous beta amyloid (A $\beta$ ) protein or autologous amyloid precursor protein (APP) in an animal~~ the method ~~reducing amyloid plaque burden in a mammal~~ comprising effecting presentation to ~~the animal's said mammal's~~ immune system of an immunogenically effective amount of ~~at least one analogue of the animal's said mammal's~~ autologous A $\beta$  or autologous APP wherein is introduced at least one isolated foreign T helper epitope (~~T<sub>H</sub> epitope~~) by means of insertion, addition, deletion, or substitution, or by means of separate coupling to a polyhydroxypolymer carrier backbone of ~~the T<sub>H</sub> epitope said foreign T helper epitope wherein said foreign T helper epitope is selected from a group consisting of Tetanus toxoid epitope, a diphtheria toxoid epitope, an influenza virus hemagglutinin epitope, a *P. falciparum* CS epitope and an artificial MCH-II binding peptide sequence; and an A $\beta$  or APP derived peptide sequence wherein said sequence is selected from the group consisting of amino acids 700-714 of SEQ ID NO:2 and amino acids 672-714 of SEQ ID NO:2, whereby immunization of the animal said mammal with the said analogue induces production of antibodies against the autologous A $\beta$  or autologous APP in the animal said mammal.~~

2. (Cancelled)

3. (Previously Presented) The method according to claim 1, wherein the introduction results in the preservation of a substantial fraction of B-cell epitopes in the A $\beta$  or APP and wherein

- at least one first moiety is introduced which effects targeting of the analogue to an antigen presenting cell (APC) or a B-lymphocyte, and/or
- at least one second moiety is introduced which stimulates the immune system, and/or
- at least one third moiety is introduced which optimizes presentation of the analogue to the immune system.

4. (Previously Presented) The method according to claim 3, wherein the analogue is modified by introducing side groups, by covalent or non-covalent binding to suitable chemical groups in A $\beta$  or APP, or a subsequence thereof, of the first and/or of the second and/or of the third moiety.
5. (Cancelled)
6. (Cancelled)
7. (Previously Presented) The method according to claim 1, wherein introduction of the amino acid substitution, deletion, insertion and/or addition results in a substantial preservation of the overall tertiary structure of A $\beta$  or APP.
8. (Previously Presented) The method according to claim 1, wherein the analogue includes a duplication of at least one B-cell epitope of the amyloidogenic polypeptide and/or an introduction of a hapten.
9. (Currently Amended) The method according to claim 1, wherein the foreign T-cell epitope is immunodominant in the ~~animal~~ mammal.
10. (Previously Presented) The method according to claim 1, wherein the foreign T-cell epitope is promiscuous.
11. (Cancelled)
12. (Previously Presented) The method according to claim 3, wherein the first moiety is selected from a substantially specific binding partner for a B-lymphocyte specific surface antigen and a substantially specific binding partner for an APC specific surface antigen.
13. (Currently Amended) The method according to claim 3, wherein the second moiety is selected from a cytokine, a hormone, and a heat-shock protein.
14. (Currently Amended) The method according to claim 3, wherein the third moiety is ~~of lipid nature~~ a lipid or wherein the third moiety is a polyhydroxypolymer.

15. (Previously Presented) The method according to claim 65, wherein the polysaccharide serves as a carrier backbone to which the A $\beta$  or APP derived peptide sequence and the foreign T cell epitope are separately bound.

16. (Previously Presented) The method according to claim 15, wherein the A $\beta$  or APP derived peptide sequence and the foreign T cell epitope are bound via an amide bond to the polysaccharide.

17. (Previously Presented) The method according to claim 1, wherein the autologous A $\beta$  or APP has been modified so as to preserve B-cell epitopes which are not exposed to the extracellular phase when present in a cell-bound form of the autologous APP.

18. (Previously Presented) The method according to claim 17, wherein the autologous A $\beta$  or APP has been modified so as to lack at least one B-cell epitope which is exposed to the extracellular phase when present in a cell-bound form of the autologous APP.

19. (Previously Presented) The method according to claim 1 which comprises a substitution of at least one amino acid sequence within autologous A $\beta$  or APP with an amino acid sequence of equal or different length which gives rise to a foreign T<sub>H</sub> epitope in the analogue.

20. (Cancelled)

21. (Cancelled)

22. (Cancelled)

23. (Cancelled)

24. (Cancelled)

25. (Previously Presented) The method according to claim 1, wherein presentation to the immune system is effected by having at least two copies of the analogue covalently ~~efor~~ non-

covalently linked to a carrier molecule capable of effecting presentation of multiple copies of antigenic determinants.

26. (Previously Presented) The method according to claim 1, wherein the analogue has been formulated with an adjuvant which facilitates breaking of autotolerance to autoantigens.

27. (Previously Presented) The method according to claim 1, wherein an effective amount of the analogue is administered to the animal via a route selected from the parenteral route; the peritoneal route; the oral route; the buccal route; the sublingual route; the epidural route; the spinal route; the anal route; and the intracranial route.

28. (Previously Presented) The method according to claim 27, wherein the effective amount is between 0.5  $\mu$ g and 2,000  $\mu$ g of the analogue.

29. (Previously Presented) The method according to claim 27, wherein the analogue is contained in a virtual lymph node (VLN) device.

30. (Cancelled)

31. (Cancelled)

32. (Cancelled)

33. (Currently Amended) The method according to ~~claims 22~~ claim 1, which includes at least one administration per year.

34. (Cancelled)

35. (Cancelled)

36. (Cancelled)

37. (Cancelled)

38. (Cancelled)

39. (Cancelled)

40. (Cancelled)

41. (Cancelled)

42. (Cancelled)

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56. (Cancelled)

57. (Cancelled)

58. (Cancelled)

59. (Previously Presented) The method according to claim 10, wherein the foreign T-cell epitope is selected from a natural promiscuous T-cell epitope and an artificial MHC-II binding peptide sequence.

60. (Currently Amended) The method according to claim ~~11~~ 1, wherein the tetanus toxoid epitope is selected from the group consisting of ~~from~~ P2 (SEQ ID NO: 4) and P30 (SEQ ID NO: 6).

61. (Currently Amended) The method according to claim 12 wherein the specific binding partner is selected from a group consisting of a hapten and a carbohydrate for which there is a receptor on the B-lymphocyte or the APC.

62. (Currently Amended) The method according to claim 13, wherein the cytokine is selected from the group consisting of interferon  $\gamma$  (IFN- $\gamma$ ), ~~an effective part of IFN- $\gamma$~~ , Flt3L, ~~an effective part of Flt3L~~, interleukin 1 (IL-1), ~~an effective part of IL-1~~, interleukin 2 (IL-2), ~~an effective part of IL-2~~, interleukin 4 (IL-4), ~~an effective part of IL-4~~, interleukin 6 (IL-6), ~~an effective part of IL-6~~, interleukin 12 (IL-12), ~~an effective part of IL-12~~, interleukin 13 (IL-13), ~~an effective part of IL-13~~, interleukin 15 (IL-15), ~~an effective part of IL-15~~, and granulocyte-macrophage colony stimulating factor (GM-CSF), ~~an effective part of GM-CSF~~.

63. (Currently Amended) The method according to claim 13, wherein the heat shock protein is selected from the group consisting of HSP70, ~~an effective part of HSP70~~, HSP90, ~~an effective part of HSP90~~, HSC70, ~~an effective part of HSC70~~, GRP94, ~~an effective part of GRP94~~, and calreticulin (CRT), ~~and an effective part of CRT~~.

64. (Currently Amended) The method according to claim 14, wherein the third moiety ~~is of lipid nature and is a lipid~~ selected from the group consisting of a palmitoyl group, a myristyl group, a farnesyl group, a geranyl-geranyl group, a GPI-anchor, and an N-acyl diglyceride group.

65. (Previously Presented) The method according to claim 14, wherein the polyhydroxypolymer is a polysaccharide.

66. (Currently Amended) The method according to claim 33, comprising at least 2 administrations per year.

67. (Currently Amended) The method according to claim 66, comprising at least 3 administrations per year.

68. (Currently Amended) The method according to claim 27, wherein the parenteral route is selected from the group consisting of the subcutaneous, the intracutaneous, and the intramuscular route.

69. (New) The method according to claim 1, wherein the artificial MHC-II binding peptide sequence is the amino acid sequence of SEQ ID NO. 19.